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         May 17 FRFULL now available on STN
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 NEWS EXPRESS
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
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=> s factor VIII-von Willebrand factor complex L2 202 FACTOR VIII-VON WILLEBRAND FACTOR COMPLEX

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L4ANSWER 1 OF 44 MEDLINE on STN

ΤI The factor VIII/von Willebrand

factor complex: basic and clinical issues.

Factor VIIII (FVIII) and von Willebrand factor (VWF) are two distinct but AΒ related glycoproteins that circulate in plasma as a tightly bound complex (FVIII/VWF). Their deficiencies or structural defects are responsible for the most common inherited bleeding disorders, namely hemophilia A (HA) and von Willebrand's disease (VWD). The VWF has a dual role in hemostasis: first it promotes platelet adhesion to thrombogenic surfaces as well as platelet-to-platelet cohesion during thrombus formation; second, it is the carrier for FVIII in plasma. FVIII acts as a co-factor to accelerate the activation of factor X by activated factor IX in the coagulation cascade. After many years of investigations, the molecular mechanisms of FVIII/VWF interactions are now well known and recent biochemical investigations have confirmed that VWF is a key partner for FVIII, playing significant roles in FVIII function, its production and its stabilization, in its conformation and immunogenicity. FVIII and VWF are both present in most plasma-derived FVIII/VWF concentrates used in clinical practice. FVIII/VWF concentrates can be classified into three main categories according to the degree of their purification.

Intermediate-high purity plasma-derived concentrates containing FVIII/VWF currently in use since 1987 carry a low risk of transmitting blood-borne infections. Concentrate safety depends on the interaction of two factors: the decrease of viral plasma load and the increase of viral inactivation. These FVIII/VWF concentrates are currently used in type 3 VWD and in type 1 or 2 VWD patients who are unresponsive to desmopressin (DDAVP). More recently the presence of the physiologic FVIII/VWF complex has been considered to play an important role also in replacement therapy for patients with HA. The correct use of FVIII/VWF concentrates in VWD and HA have been reported in several national and international guidelines.

2003, Ferrata Storti Foundation

ACCESSION NUMBER: 2003299060 MEDLINE PubMed ID: 12826528 DOCUMENT NUMBER: TITLE: The factor VIII/von

Willebrand factor complex: basic and clinical issues.

AUTHOR:

Federici Augusto B

CORPORATE SOURCE: Angelo Bianchi Bonomi Hemophilia Thrombosis Center,

Department of Internal Medicine, IRCCS Maggiore Hospital and University of Milan, Italy.. augusto.federici@unimi.it Haematologica, (2003 Jun) 88 (6) EREP02. Ref: 40

SOURCE:

Journal code: 0417435. ISSN: 1592-8721.

PUB. COUNTRY: Italy

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200401

ENTRY DATE: Entered STN: 20030627

Last Updated on STN: 20040130 Entered Medline: 20040129

ANSWER 2 OF 44 MEDLINE on STN T.4

ΤI Isolation of the factor VIII-von

> Willebrand factor complex directly from plasma by gel filtration.

A high capacity gel filtration system was developed with the purpose of AB isolating factor VIII (FVIII) and von Willebrand factor (vWF) directly from plasma in significantly higher yields than obtained by cryoprecipitation, the technique most commonly used to recover FVIII-vWF from human plasma. After laboratory-scale gel filtration of plasma, a FVIII-containing fraction was collected containing about 90% of FVIII in the applied plasma and with almost tenfold higher purity than that obtained by cryoprecipitation. The gel filtration step has been scaled up for use as the initial step in the manufacturing process for a FVIII

preparation (Nordiate).

ACCESSION NUMBER: 1999007008 MEDLINE DOCUMENT NUMBER: PubMed ID: 9792522

TITLE: Isolation of the factor VIII-

von Willebrand factor

complex directly from plasma by gel filtration.

load date

AUTHOR: Kaersgaard P; Barington K A

CORPORATE SOURCE: HemaSure Denmark A/S, Gentofte.

SOURCE: Journal of chromatography. B, Biomedical sciences and

applications, (1998 Sep 18) 715 (2) 357-67. Journal code: 9714109. ISSN: 1387-2273.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199812

ENTRY DATE: Entered STN: 19990115

Last Updated on STN: 19990115 Entered Medline: 19981218

L4 ANSWER 3 OF 44 MEDLINE on STN

TI Application of a new statistical approach to optimize the immunopurification of antihemophilia A factor.

AB Our aim was to optimize the immunopurification process of human factor VIII. This purification was performed using a mouse monoclonal anti-factor VIII light-chain antibody. Previous dissociation of the factor VIII-von Willebrand

factor complex with CaCl2 led to a 50% increase of the factor VIII adsorption on the immunosorbent. The optimization of the elution step required the analysis of the effects of two parameters, pH and ionic strength, on four different responses: elution yield, concentration, specific activity and stability of factor VIII. For this purpose, a multifunctional method using Doehlert matrices for statistically designed experiments was applied. This methodology allowed us to obtain, with only seven experiments, a 60% increase of the elution yield and a two-fold increase of the specific activity of factor VIII.

ACCESSION NUMBER: 93203403 MEDLINE DOCUMENT NUMBER: PubMed ID: 8454702

TITLE: Application of a new statistical approach to optimize the

immunopurification of antihemophilia A factor.

AUTHOR: Bihoreau N; Layet S; Fontaine-Aupart M P; Paolantonacci P

CORPORATE SOURCE: T.M. Innovation (Centre National de Transfusion

Sanguine-Institut Merieux, Les Ulis, France.

SOURCE: Journal of chromatography, (1993 Jan 29) 612 (1) 49-56.

Journal code: 0427043. ISSN: 0021-9673.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199304

ENTRY DATE: Entered STN: 19930507

Last Updated on STN: 19970203 Entered Medline: 19930422

L4 ANSWER 4 OF 44 MEDLINE on STN

TI The interaction of the factor VIII/von Willebrand factor complex (VIII/vWf), with

guanidinium-derivatized matrices.

Five different quanidinium (Gu)-der

AB Five different guanidinium (Gu)-derivatized agarose matrices were investigated for their potential in chromatographically resolving the Factor VIII/von Willebrand complex, VIII/vWf, fibrinogen, Fg, and

fibronectin, Fn, from cryoprecipitate. Using conventional NaCl gradient methodology it was found that the order of elution of specific plasma proteins, and the yield of VIII/vWf, varied with the methods used to derivatize the agarose beads. Good yields of VIII:C (generally 30-45%) were obtained with Gu-matrices prepared by bis-oxirane coupling procedures. Cryoprecipitate binding studies showed that the capacity of Gu-Sepharose 4B, prepared by isourea modification of amino-Sepharose 4B, was 36 units VIII/vWf per ml matrix. The product, depleted of both Fg and Fn, had a specific activity of 2 units VIII:C per mg total protein, (yield 100% vWf:Aq and 47% VIII:C).

ACCESSION NUMBER: DOCUMENT NUMBER:

92240106 MEDLINE PubMed ID: 1368084

TITLE:

The interaction of the factor VIII/

von Willebrand factor

complex (VIII/vWf), with guanidinium-derivatized

matrices.

AUTHOR:

Saundry R H; Savidge G F

CORPORATE SOURCE:

Coagulation Research Laboratory, Rayne Institute, St.

Thomas' Hospital, London, UK.

SOURCE:

Bioseparation, (1991) 2 (3) 177-86.

Journal code: 9011423. ISSN: 0923-179X.

PUB. COUNTRY:

Netherlands

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT:

Biotechnology

ENTRY MONTH:

199206

ENTRY DATE:

Entered STN: 19950809

Last Updated on STN: 19980206 Entered Medline: 19920602

L4 ANSWER 5 OF 44 MEDLINE on STN

TI Topography of the human factor VIII-von

Willebrand factor complex.

Factor VIII circulates in noncovalent complex with von Willebrand factor (vWf). The topography of this complex was evaluated by fluorescence energy transfer using factor VIII subunits modified with N-(1-pyrenyl) maleimide (NPM; fluorescence donor) and vWf-derived fragments modified with 7-diethylamino-3-[4'-maleimidylphenyl]-4-methyl coumarin (CPM; fluorescence acceptor). Results from a previous study indicated an interfactor VIII subunit distance of 20 A separating Cys528 and Cys1858 in the factor VIII heavy and light chains, respectively (Fay, P.J., and Smudzin, T. M. (1989) J. Biol. Chemical 264, 14005-14010). Fluorophore modification of the vWf SPIII homodimer (residues 1-1365) indicated multiple attachment sites at Cys126/135/1360 as determined from sequence analysis of fluorescent tryptic peptides derived from the modified protein. Based upon donor quenching data, an interfluorophore distance of approximately 28 A was calculated separating NPM-factor VIII light chain or factor VIII reconstituted from NPM-light chain plus unmodified heavy chain, from CPM-SPIII. A similar value (29 A) was obtained for NPM-light chain paired with CPM-SPIII-T4 (vWf residues 1-272), suggesting that donor quenching resulted primarily from modified residue(s) Cys126/135 in the acceptor. No energy transfer was observed for the NPM-heavy chain/CPM-SPIII pairing. However, when NPM-heavy chain was reassociated with unmodified light chain prior to reaction with CPM-SPIII or CPM-SPIII-T4, energy transfer was observed with calculated interfluorophore distances of approximately 31 and 34 A, respectively. Levels of acceptor resulting in maximal donor quenching suggested an equimolar stoichiometry of factor VIII (light chain)/vWf fragment in the reconstituted complexes. These results indicate a close spatial arrangement among the A3 domain of factor VIII light chain, the A2 domain of factor VIII heavy chain, and the NH2 terminus region of vWf in the factor VIII-vWf complex.

ACCESSION NUMBER: 90202891 MEDLINE DOCUMENT NUMBER: PubMed ID: 2108154

TITLE: Topography of the human factor VIII-

von Willebrand factor

complex.

AUTHOR: Fay P J; Smudzin T M

CORPORATE SOURCE: Department of Medicine, University of Rochester School of

Medicine and Dentistry, New York 14642.

CONTRACT NUMBER: HL-38199 (NHLBI)

SOURCE: Journal of biological chemistry, (1990 Apr 15) 265 (11)

6197-202

Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199005

ENTRY DATE: Entered STN: 19900601

Last Updated on STN: 19900601 Entered Medline: 19900510

L4 ANSWER 6 OF 44 MEDLINE on STN

TI Differential proteolytic activation of factor VIII-

von Willebrand factor complex by

thrombin.

Blood coagulation factor VIII (fVIII) is a plasma protein that is ΔB decreased or absent in hemophilia A. It is isolated as a mixture of heterodimers that contain a variably sized heavy chain and a common light Thrombin catalyzes the activation of fVIII in a reaction that is associated with cleavages in both types of chain. We isolated a serine protease from Bothrops jararacussu snake venom that catalyzes thrombin-like heavy-chain cleavage but not light-chain cleavage in porcine fVIII as judged by NaDodSO4/PAGE and N-terminal sequence analysis. Using a plasma-free assay of the ability of activated fVIII to function as a cofactor in the activation of factor X by factor IXa, we found that fVIII is activated by the venom enzyme. The venom enzyme-activated fVIII was isolated in stable form by cation-exchange HPLC. von Willebrand factor inhibited venom enzyme-activated fVIII but not thrombin-activated fVIII. These results suggest that the binding of fVIII to von Willebrand factor depends on the presence of an intact light chain and that activated fVIII must dissociate from von Willebrand factor to exert its cofactor effect. Thus, proteolytic activation of fVIII-von Willebrand factor complex appears to be differentially regulated by light-chain cleavage to dissociate the complex and heavy-chain cleavage to activate the cofactor function.

ACCESSION NUMBER: 89367278 MEDLINE DOCUMENT NUMBER: PubMed ID: 2505252

TITLE: Differential proteolytic activation of factor

VIII-von Willebrand

factor complex by thrombin.

AUTHOR: Hill-Eubanks D C; Parker C G; Lollar P

CORPORATE SOURCE: Department of Biochemistry, University of Vermont,

Burlington 05405.
CONTRACT NUMBER: HL-35058 (NHLBI)

HL-40921 (NHLBI)

SOURCE: Proceedings of the National Academy of Sciences of the

United States of America, (1989 Sep) 86 (17) 6508-12.

Journal code: 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198910

ENTRY DATE: Entered STN: 19900309

Last Updated on STN: 19970203 Entered Medline: 19891006 L4 ANSWER 7 OF 44 MEDLINE on STN

TI Characteristics of the von Willebrand factor in virus inactivated F VIII concentrates: the impact of heat treatment.

AB The known transmission of viral diseases, particularly AIDS (HIV, LAV, HTLV-III), has led to the mandatory use of virus-inactivated coagulation factor concentrates for treatment of bleeding disorders due to deficient or abnormal synthesis of the factor VIII/von

Willebrand factor complex. The present

investigation was undertaken to study the influence of heat-treatment on the von Willebrand factor (vWf). Using normal plasma as reference material, we studied the influence of low-purification steps in a simple cryo-plasma and a unrefined freeze-dried cryoprecipitate. For comparison, non-heated and heat-inactivated concentrates of different manufacture representing varying heat-treatment protocols were studied using quantitation of von Willebrand factor antigen (vWf:Ag) by electroimmunoassay and ELISA, and investigation of vWf multimeric composition. A locally produced factor VIII concentrate was studied before and after exposure to 68 degrees C for 72 hours (dry state). Whenever possible, commercial preparations manufactured prior to the heat-treatment era were compared with the present product. The locally produced high purity concentrate elicited only minor changes in oligomeric satellite pattern, which did not change after dry heat exposure. In principle, no major differences were found between non-heated and pasteurized commercial concentrates of same manufactural origin.

ACCESSION NUMBER: 88018700

DOCUMENT NUMBER: PubMed ID: 3116714

TITLE: Characteristics of the von Willebrand factor in virus

MEDLINE

inactivated F VIII concentrates: the impact of heat

treatment.

AUTHOR: Ingerslev J; Bukh A; Wallevik K; Moller N P; Stenbjerg S

CORPORATE SOURCE: Department of Clinical Immunology, University Hospital

Aarhus, Denmark.

SOURCE: Thrombosis research, (1987 Jul 15) 47 (2) 175-82.

Journal code: 0326377. ISSN: 0049-3848.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; AIDS

ENTRY MONTH: 198710

ENTRY DATE: Entered STN: 19900305

Last Updated on STN: 19900305 Entered Medline: 19871028

L4 ANSWER 8 OF 44 MEDLINE on STN

TI Investigation of a coagulation accelerating factor (CAF) in glomerulonephritis.

AB A coagulation accelerating factor was purified from the plasma of two patients with glomerulonephritis (GN) who suffered from thrombotic complications. The factor co-purified with factor VIII

/von Willebrand factor complex

(FVIII/vWf) and under dissociating conditions remained associated with the factor VIII coagulant activity (FVIII). Control purified FVIII/vWf showed no coagulation accelerating activity under the experimental conditions used. The levels of coagulation accelerating factor, FVIII and von Willebrand factor (vWf) were reduced by incubation with rabbit anti-human FVIII/vWf or human anti-FVIII serum indicating a close association of these three activities. Multimeric analysis of the plasma FVIII/vWf complex from the two patients demonstrated a reduction in the high molecular weight multimers and the presence of an additional band not present on analysis of normal FVIII/vWf. It is suggested that the coagulation accelerating factor represents an active form of FVIII which has different in vitro properties to thrombin activated FVIII.

ACCESSION NUMBER: 85122559 MEDLINE

DOCUMENT NUMBER:

PubMed ID: 3918561

TITLE:

Investigation of a coagulation accelerating factor (CAF) in

glomerulonephritis.

AUTHOR:

Salem H H; Howard M A; Koutts J; Firkin B G

SOURCE:

British journal of haematology, (1985 Mar) 59 (3) 485-96.

Journal code: 0372544. ISSN: 0007-1048.

PUB. COUNTRY:

ENGLAND: United Kingdom

DOCUMENT TYPE:

(CASE REPORTS)

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

198504

ENTRY DATE:

Entered STN: 19900320

Last Updated on STN: 19900320 Entered Medline: 19850423

ANSWER 9 OF 44 USPATFULL on STN L4

TT Method for producing a factor VIII/von

Willebrand factor complex

AB

The invention relates to a method for the production of factor VIII: C/von Willebrand factor complex from plasma or a plasma fraction by chromatography in a cation exchanger, wherein the factor VIII: C/von Willebrand factor complex is obtained with at least 300 times the purity of the plasma and the yield of factor VIII: C and the von Willebrand factor is at least 50% in relation to cryoprecipitates or analogous plasma fractions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:

2003:215997 USPATFULL

TITLE:

Method for producing a factor VIII/

von Willebrand factor

complex

INVENTOR(S):

Linnau, Yendra, Vienna, AUSTRIA

Schoenhofer, Wolfgang, St. Poelten, AUSTRIA

PATENT ASSIGNEE(S):

Baxter Aktiengesellschaft, Vienna, AUSTRIA (non-U.S.

had date

corporation)

| PATENT | INFORMATION: | <u>U</u> S |
|--------|--------------|------------|
| | | |

| | NUMBER | KIND | DATE | |
|----|-------------|------|----------|--|
| us | 6605222 | B1 | 20030812 | |
| WO | 9943712 | | 19990902 | |
| US | 2001-623245 | | 20010319 | |

APPLICATION INFO .:

(9) WO 1999-AT48 19990225

NUMBER _____

PRIORITY INFORMATION:

AT 1998-866 19980520

DOCUMENT TYPE:

Utility

FILE SEGMENT:

GRANTED

PRIMARY EXAMINER:

LEGAL REPRESENTATIVE:

Therkorn, Ernest G.

NUMBER OF CLAIMS:

Townsend and Townsend and Crew LLP, Fedrick, Michael F.

EXEMPLARY CLAIM:

NUMBER OF DRAWINGS:

0 Drawing Figure(s); 0 Drawing Page(s)

LINE COUNT:

203

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4ANSWER 10 OF 44 USPATFULL on STN

Controllable ion-exchange membranes ΤI

Multilayered porous materials are formed by coating a porous substrate AB with a metal and adsorbing an organic layer comprising a recognition moiety onto the metal film. The recognition moiety interacts with an analyte of interest allowing for its detection, purification, etc. Suitable recognition moieties can be selected from a range of

species including, small molecules, polymers and biomolecules and the like. The novel porous materials of the invention can be utilized in an array of methods including, ion-exchange, ion-selective ion-exchange, assays, affinity dialysis, size exclusion dialysis and the like.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

2002:275837 USPATFULL ACCESSION NUMBER:

Controllable ion-exchange membranes TITLE: Hou, Zhizhong, Davis, CA, United States INVENTOR(S): Stroeve, Pieter, Davis, CA, United States

Abbott, Nicholas, Madison, WI, United States

(9)

(,30 7032

The Regents of the University of California, Oakland, PATENT ASSIGNEE(S):

CA, United States (U.S. corporation)

KIND DATE NUMBER ______ US 6468657 B1 20021022 PATENT INFORMATION: 19981204 US 1998-206084 APPLICATION INFO.:

DOCUMENT TYPE: Utility FILE SEGMENT: GRANTED

PRIMARY EXAMINER: Le, Hoa T. Townsend and Townsend and Crew LLP LEGAL REPRESENTATIVE:

NUMBER OF CLAIMS: 71 EXEMPLARY CLAIM:

6 Drawing Figure(s); 4 Drawing Page(s) NUMBER OF DRAWINGS:

LINE COUNT: 3454

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 11 OF 44 USPATFULL on STN

Von willebrand factor derivatives and methods of isolating proteins that TТ bind to von willebrand factor

There is disclosed a vWF derivative comprised of vWF, immobilized on a AB carrier, which is characterized in that the vWF is r-vWF, as well as a method of isolating proteins which bind to vWF, by using this vWF derivative.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:32215 USPATFULL

Von willebrand factor derivatives and methods of TITLE:

isolating proteins that bind to von willebrand factor

Schwarz, Hans-Peter, Vienna, AUSTRIA INVENTOR(S):

Turecek, Peter, Klosterneuburg, AUSTRIA

Eibl, Johann, Vienna, AUSTRIA

NUMBER KIND DATE ______ US 2002019036 A1 20020214 US 2001-967937 A1 20011002 (9) US 2002019036 PATENT INFORMATION: APPLICATION INFO.:

Division of Ser. No. US 1999-319116, filed on 2 Jun RELATED APPLN. INFO.: 1999, PENDING A 371 of International Ser. No. WO

1997-AT253, filed on 19 Nov 1997, UNKNOWN

NUMBER DATE PRIORITY INFORMATION: AT 1996-2178 19961213

DOCUMENT TYPE: Utility APPLICATION FILE SEGMENT:

LEGAL REPRESENTATIVE: HELLER EHRMAN WHITE & MCAULIFFE LLP, 1666 K STREET, NW,

SUITE 300, WASHINGTON, DC, 20006

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 2 Drawing Page(s)

598 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 12 OF 44 USPATFULL on STN L4

Proteins with factor VIII activity: process for their preparation using ΤI genetically-engineered cells and pharmaceutical compositions containing

Novel polypeptides having Factor VIII activity are provided as well as AB compositions and methods for their preparation. The polypeptides comprise derivatives and fragments of Factor VIII and have sequences substantially similar to portions of naturally occuring Factor VIII. The polypeptides find use in treatment of Hemophilia A.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:

2002:29368 USPATFULL

TITLE:

Proteins with factor VIII activity: process for their preparation using genetically-engineered cells and

pharmaceutical compositions containing them

INVENTOR(S):

Van Ooyen, Albert Johannes Joseph, Voorburg,

NETHERLANDS

Pannekoek, Hans, Aalsmeer, NETHERLANDS

Verbeet, Martinus Philippus, Amsterdam, NETHERLANDS

Van Leen, Robert Willem, Nijmegen, NETHERLANDS Baxter Trading GmbH, Vienna, AUSTRIA (non-U.S.

PATENT ASSIGNEE(S):

corporation)

NUMBER KIND DATE ______ US 6346513 B1 20020212 US 1995-416535 19950403 (8)

PATENT INFORMATION: APPLICATION INFO.:

RELATED APPLN. INFO.:

Continuation of Ser. No. US 1994-272947, filed on 11 Jul 1994, now abandoned Continuation of Ser. No. US 1992-879328, filed on 7 May 1992, now abandoned Continuation of Ser. No. US 1998-205226, filed on 10

Jun 1998, now patented, Pat. No. US 5171844

NUMBER DATE ______

PRIORITY INFORMATION:

EP 1987-U2011218 19870612

DOCUMENT TYPE:

Utility

FILE SEGMENT:

GRANTED

PRIMARY EXAMINER:

Low, Christopher S.F.

ASSISTANT EXAMINER:

Schnizer, Holly

LEGAL REPRESENTATIVE:

Heller Ehrman White & McAuliffe

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

1

NUMBER OF DRAWINGS:

18 Drawing Figure(s); 12 Drawing Page(s) LINE COUNT: 1130

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 13 OF 44 USPATFULL on STN L4

Proteins with Factor VIII activity: process for their preparation using ΤI genetically-engineered cells and pharmaceutical compositions containing them

Novel polypeptides having Factor VIII activity are provided as well as AB compositions and methods for their preparation. The polypeptides comprise derivatives and fragments of Factor VIII and have sequences substantially similar to portions of naturally occuring Pactor VIII. The polypeptides find use in treatment of Hemophilia A.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:

2001:202415 USPATFULL

TITLE:

Proteins with Factor VIII activity: process for their

preparation using genetically-engineered cells and pharmaceutical compositions containing them

INVENTOR(S):

Van Ooyen, Albert Johannes Joseph, Voorburg,

Netherlands

Pannekoek, Hans, Aalsmeer, Netherlands

Verbeet, Martinus Philippus, Amsterdam, Netherlands Van Leen, Robert Willem, Nijmegen, Netherlands

PATENT ASSIGNEE(S):

Baxter Trading GmbH, Vienna, Australia (non-U.S.

corporation)

NUMBER KIND DATE _____ US 6316226 B1 20011113 PATENT INFORMATION: US 1995-416532 19950403 (8) APPLICATION INFO.:

RELATED APPLN. INFO.: Continuation of Ser. No. US 1994-272952, filed on 11

Jul 1994, now abandoned Continuation of Ser. No. US 1992-990895, filed on 15 Dec 1992, now abandoned Division of Ser. No. US 1988-205226, filed on 10 Jun

1988, now patented, Pat. No. US 5171844

DATE NUMBER ______

PRIORITY INFORMATION: EP 1987-201121 19870612

DOCUMENT TYPE: Utility GRANTED FILE SEGMENT:

Low, Christopher S. F. PRIMARY EXAMINER:

ASSISTANT EXAMINER: Schnizer, Holly

LEGAL REPRESENTATIVE: Heller Ehrman White & McAuliffe

Я NUMBER OF CLAIMS: EXEMPLARY CLAIM:

AB

18 Drawing Figure(s); 12 Drawing Page(s) NUMBER OF DRAWINGS:

1176 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 14 OF 44 USPATFULL on STN L4TI

Support for high performance affinity chromatography and other uses Multilayered particulate materials are formed by coating a particulate substrate with a metal and adsorbing an organic layer comprising a recognition moiety onto the metal film. The recognition moiety interacts with an analyte of interest allowing for its detection, purification, etc. Suitable recognition moieties can be selected from a range of species including, small molecules, polymers and biomolecules and the like. The novel particulate materials of the invention can be utilized in an array of methods including, ion-exchange, ion-selective ion-exchange, assays, affinity dialysis, size exclusion dialysis, as supports in solid phase synthesis, combinatorial synthesis and screening of compound libraries and the like.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

2001:136295 USPATFULL ACCESSION NUMBER:

Support for high performance affinity chromatography TITLE:

and other uses

Abbott, Nicholas, Madison, WI, United States INVENTOR(S):

Stroeve, Pieter, Davis, CA, United States

Dubrovsky, Timothy B., Flemington, NJ, United States

Hou, Zhizhong, Davis, CA, United States

The Regents of the University of California, Oakland, PATENT ASSIGNEE(S):

CA, United States (U.S. corporation)

NUMBER KIND DATE US 6277489 B1 20010821 PATENT INFORMATION: US 1998-205750 19981204 (9) APPLICATION INFO.: DOCUMENT TYPE: Utility

FILE SEGMENT: GRANTED Le, Hoa T. PRIMARY EXAMINER:

Townsend and Townsend and Crew LLP LEGAL REPRESENTATIVE:

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)

LINE COUNT: 3868

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 15 OF 44 USPATFULL on STN

Stable factor VIII/von Willebrand TI

factor complex

There are disclosed a stable factor VIII/vWF-complex, particularly AB comprising high-molecular vWF multimers, being free from low-molecular vWF molecules and from proteolytic vWF degradation products, as well as a method of producing this complex.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:

2001:67424 USPATFULL

TITLE:

Stable factor VIII/von Willebrand factor complex

INVENTOR(S):

Fischer, Bernhard, Vienna, Austria Mitterer, Artur, Mannsdorf, Austria Dorner, Friedrich, Vienna, Austria

Eibl, Johann, Vienna, Austria

PATENT ASSIGNEE(S):

Baxter Aktiengesellschaft, Vienna, Austria (non-U.S.

corporation)

| | NUMBER | KIND | DATE | |
|---------------------|---------------------|------|----------|-----------------|
| | | | | |
| PATENT INFORMATION: | US 62 <u>286</u> 13 | B1 | 20010508 | |
| | WO 9734930 | | 19970925 | |
| APPLICATION INFO.: | US 1998-142768 | | 19981106 | (9) |
| | WO 1997-AT55 | | 19970313 | |
| | | | 19981106 | PCT 371 date |
| | | | 19981106 | PCT 102(e) date |

NUMBER DATE

PRIORITY INFORMATION:

AT 1996-494 19960315

DOCUMENT TYPE: FILE SEGMENT:

Utility Granted

PRIMARY EXAMINER:

Carlson, Karen Cochrane

ASSISTANT EXAMINER:

Robinson, Hope A.

LEGAL REPRESENTATIVE:

Heller Ehrman White & McAuliffe

NUMBER OF CLAIMS:

EXEMPLARY CLAIM:

40 1

NUMBER OF DRAWINGS:

9 Drawing Figure(s); 9 Drawing Page(s)

LINE COUNT:

1098

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 16 OF 44 USPATFULL on STN L4

Fibrinogen concentrate obtained from blood plasma, process and plant for ΤI its preparation

A fibrinogen concentrate has a purity of 98% or higher and is free of AB viral contaminants and proteases. The fibrinogen concentrate is obtained by subjecting a solubilized plasma fraction containing fibrinogen to a viral inactivation chemical treatment using a solvent/detergent, subjecting the resulting viral-inactivated fraction to precipitation in a solution containing an amino acid at an acidic pH to obtain a supernatant, filtering the supernatant to obtain a purified fibrinogen concentrate, and recovering the purified fibrinogen concentrate.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:

1998:138854 USPATFULL

TITLE:

Fibrinogen concentrate obtained from blood plasma,

process and plant for its preparation

INVENTOR(S): Laub, Ruth, Brussels, Belgium

Wael, Luc De, Ranst, Belgium

PATENT ASSIGNEE(S): Croix-Rouge de Belgique, Brussels, Belgium (non-U.S.

corporation)

WO 1995-BE69 19950714

19970707 PCT 371 date 19970707 PCT 102(e) date

NUMBER DATE

PRIORITY INFORMATION: EP 1995-94870121 19950823

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted

PRIMARY EXAMINER: Tsang, Cecilia J. ASSISTANT EXAMINER: Marshall, S. G.

LEGAL REPRESENTATIVE: Knobbe, Martens, Olson and Bear, LLP

NUMBER OF CLAIMS: 16 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)

LINE COUNT: 553

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 17 OF 44 USPATFULL on STN

TI Antiplasma animal model

There is disclosed an anti-plasma antibody preparation for treatment of a mammal, which preparation is capable of directly or indirectly inhibiting and/or eliminating several blood factors, a method of producing such a preparation and a method of evaluating substances for treating clotting disorders by using said anti-plasma antibody preparation. There is further disclosed a method of determining the bleeding characteristics of a mammal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 1998:107999 USPATFULL TITLE: Antiplasma animal model

INVENTOR(S):

Antiplasma animal model

Eibl, Johann, Vienna, Austria

Turecek, Peter, Klosterneuburg Weidling, Austria

Schwarz, Hans Peter, Vienna, Austria

PATENT ASSIGNEE(S): Immuno Aktiengesellschaft, Vienna, Austria (non-U.S.

corporation)

NUMBER DATE

PRIORITY INFORMATION: AT 1995-987 19950609
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted

PRIMARY EXAMINER: Chambers, Jasemine C.

ASSISTANT EXAMINER: Hauda, Karen M. LEGAL REPRESENTATIVE: Foley & Lardner

NUMBER OF CLAIMS: 3 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 7 Drawing Figure(s); 7 Drawing Page(s)

LINE COUNT: 737

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 18 OF 44 USPATFULL on STN L4

Process for preparing a concentrate of blood coagulation factor TТ

VIII-von willebrand factor complex from total plasma

The invention relates to a process for preparing a concentrate of AB

Factor VIII-von Willebrand

factor complex having high specific activity from

total (non-cryoprecipitated) plasma.

The process comprises pre-purifying by means of a double treatment with barium chloride and with aluminium hydroxide.

The process then comprises purification by chromatography on an anion exchange resin, of the DEAE-Fractogel type.

The process includes a step of viral inactivation by means of a treatment with solvent-detergent.

The process also makes it possible to recover fibrinogen, albumin, immunoglobulins, antithrombin III, fibronectin and prothrombin complex, from the same plasma.

The different concentrates obtained using the process according to the invention are intended, in particular, for therapeutic use.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:

97:96964 USPATFULL

TITLE:

Process for preparing a concentrate of blood

coaquiation factor VIII-von willebrand factor complex

from total plasma

INVENTOR (S):

Burnouf-Radosevich, Miryana, Wavrin, France

Burnouf, Thierry, Wavrin, France

PATENT ASSIGNEE(S):

Centre Regional de Transfusion Sanguine de Lille,

Lille, France (non-U.S. corporation)

NUMBER KIND US 5679776 US 1990-577368 19971021 PATENT INFORMATION: 19900905 (7) APPLICATION INFO.:

> NUMBER DATE _____

PRIORITY INFORMATION:

FR 1989-11567 19890905

DOCUMENT TYPE:

Utility

Granted FILE SEGMENT:

Hendricks, Keith D.

PRIMARY EXAMINER: ASSISTANT EXAMINER:

Moore, W.

LEGAL REPRESENTATIVE:

Birch, Stewart, Kolasch & Birch, LLP

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

20 1

LINE COUNT: 406

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 19 OF 44 USPATFULL on STN L4

ELISA using multi-species antibodies for detection of von Willebrand TΙ

factor in multiple species

The subject invention provides an antibody directed to von Willebrand AB factor antigen characterized by being capable of recognizing an epitope of the von Willebrand factor antigen, the epitope being evolutionarily conserved among vertebrate species. The subject invention further

provides a method for the qualitative and quantitative detection of von Willebrand factor in multiple species using an enzyme-linked immunosorbent assay and the antibodies of the subject invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 93:29142 USPATFULL

TITLE: ELISA using multi-species antibodies for detection of

von Willebrand factor in multiple species

INVENTOR(S): Benson, Roger E., Albany, NY, United States

Catalfamo, James L., South Bethlehem, NY, United States

Dodds, W. Jean, Santa Monica, CA, United States

PATENT ASSIGNEE(S): Health Research, Incorporated, Albany, NY, United

States (U.S. corporation)

PATENT INFORMATION: US 5202264 19930413
APPLICATION INFO.: US 1990-604885 19901026 (7)

DISCLAIMER DATE: 20100323

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1990-428161, filed

on 11 Jan 1990

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Nucker, Christine M. ASSISTANT EXAMINER: Woodward, M. P. LEGAL REPRESENTATIVE: Heslin & Rothenberg

NUMBER OF CLAIMS: 85 EXEMPLARY CLAIM: 1

INVENTOR(S):

NUMBER OF DRAWINGS: 12 Drawing Figure(s); 12 Drawing Page(s)

LINE COUNT: 2442

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 20 OF 44 USPATFULL on STN

TI Proteins with factor VIII activity: process for their preparation using genetically-engineered cells and pharmaceutical compositions containing them

AB Novel polypeptides having Factor VIII activity are provided as well as compositions and methods for their preparation. The polypeptides comprise derivatives and fragments of Factor VIII and have sequences substantially similar to portions of naturally occurring Factor VIII. The polypeptides find use in treatment of Hemophilia A.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 92:103157 USPATFULL

TITLE: Proteins with factor VIII activity: process for their

preparation using genetically-engineered cells and

pharmaceutical compositions containing them van Ooyen, Albert J. J., Voorburg, Netherlands

Pannekoek, Hans, Aalsmeer, Netherlands

Verbeet, Martinus P., Amsterdam, Netherlands van Leen, Robert W., Nijmegen, Netherlands

PATENT ASSIGNEE(S): Gist-Brocades N.W., Delft, Netherlands (non-U.S.

corporation)

NUMBER DATE

PRIORITY INFORMATION: EP 1987-201121 19870612

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

Wax, Robert A. PRIMARY EXAMINER: Baker, R. Keith ASSISTANT EXAMINER: Rae-Venter, Barbara LEGAL REPRESENTATIVE:

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

18 Drawing Figure(s); 12 Drawing Page(s) NUMBER OF DRAWINGS:

LINE COUNT: 1081

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 21 OF 44 USPATFULL on STN

Purification of von Willebrand Factor by affinity TT

chromatography

A method of preparing von Willebrand Factor by disassociating it from a AB chaotropic agent in solution therewith and preferably treating the same under controlled temperature either in liquid or lyophilized form.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. ACCESSION NUMBER: 91:28708 USPATFULL

Purification of von Willebrand Factor by TITLE:

affinity chromatography

Newman, Jack, Burke, VA, United States INVENTOR(S):

Farb, David L., Woodbridge, VA, United States

Rhone-Poulenc Rorer Pharmaceuticals Inc., Fort PATENT ASSIGNEE(S):

Washington, PA, United States (U.S. corporation)

NUMBER KIND DATE -----US 5006642 19910409 US 1988-205881 19880613 (7) PATENT INFORMATION: APPLICATION INFO.:

RELATED APPLN. INFO.: Division of Ser. No. US 1987-67990, filed on 29 Jun

1987, now patented, Pat. No. US 4774323

Utility DOCUMENT TYPE: Granted FILE SEGMENT:

Moskowitz, Margaret PRIMARY EXAMINER: ASSISTANT EXAMINER:

Furman, Keith C.
Balogh, Imre (Jim), Nicholson, James A. LEGAL REPRESENTATIVE:

NUMBER OF CLAIMS: 12 EXEMPLARY CLAIM: 1 LINE COUNT: 415

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 22 OF 44 USPATFULL on STN L4

Biologically active fragments of human antihemophilic factor and method ΤI for preparation thereof

Novel, biologically active fragments of human antihemophilic factor, AB processes for their preparation, pharmaceutical preparations containing them and the use of such fragments in the treatment of patients suffering from hemophilia.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. 89:89037 USPATFULL ACCESSION NUMBER:

Biologically active fragments of human antihemophilic TITLE:

factor and method for preparation thereof

INVENTOR(S): Andersson, Lars-Olof, Knivsta, Sweden

Forsman, Nanna, Jarfalla, Sweden Larsen, Kerstin E. I., Lidingo, Sweden Lundin, Annelie B., Stockholm, Sweden

Pavlu, Bohdan, Huddinge, Sweden Sandberg, Inga H., Spånga, Sweden Sewerin, Karin M., Bromma, Sweden

PATENT ASSIGNEE(S): Kabivitrum AB, Stockholm, Sweden (non-U.S. corporation)

> NUMBER KIND DATE

PATENT INFORMATION: US 4877614 APPLICATION INFO.:

US 1988-185629

19891031 19880425 (7)

NUMBER

DATE

PRIORITY INFORMATION:

SE 1985-1050 19850305

DOCUMENT TYPE: FILE SEGMENT:

Utility Granted

PRIMARY EXAMINER:

Kight, John

ASSISTANT EXAMINER:

Nutter, Nathan M.

LEGAL REPRESENTATIVE:

Pollock, Vande Sande & Priddy

NUMBER OF CLAIMS:

EXEMPLARY CLAIM:

NUMBER OF DRAWINGS:

5 Drawing Figure(s); 3 Drawing Page(s)

LINE COUNT:

881

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 23 OF 44 USPATFULL on STN

Flouroplastic immunoaffinity columns for purification of blood ΤI

proteins

AB

The present invention is a protein purification column comprising an organic substrate matrix having low reactivity to proteins, said matrix being capable of maintaining monoclonal antibodies attached thereto in an external configuration and preventing interaction with the protein to be bound to the antibody, and a monoclonal antibody attached to the substrate, the monoclonal antibody having a specific affinity for the protein to be isolated.

The present invention also is a method for isolating and purifying specific protein from a solution, wherein

- 1. Protein-specific monoclonal antibody is attached to the organic substrate matrix described above to form an antibody-substrate conjugate; and
- 2. Protein to be isolated, in an appropriate buffer solution, is contacted with the antibody-substrate conjugate.

An appropriate buffer may be applied to remove non-antibody bound contaminants, followed by an appropriate eluting agent to remove the protein from the monoclonal antibody.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:

89:39057 USPATFULL

TITLE:

Flouroplastic immunoaffinity columns for

purification of blood proteins

INVENTOR(S):

Zimmerman, Theodore S., La Jolla, CA, United States

Fulcher, Carol A., La Jolla, CA, United States

Scripps Clinic and Research Foundation, La Jolla, CA, PATENT ASSIGNEE(S):

United States (U.S. corporation)

NUMBER KIND DATE US 4831118 19890516 PATENT INFORMATION:

APPLICATION INFO.:

US 1987-83670

19870807 (7)

DOCUMENT TYPE:

Utility Granted

FILE SEGMENT: PRIMARY EXAMINER: Moskowitz, Margaret ASSISTANT EXAMINER: Kushan, Jeff P. LEGAL REPRESENTATIVE: Morgan & Finnegan

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

17 1

377 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 24 OF 44 USPATFULL on STN **L4**

Biologically active fragments of human antihemophilic factor and method TI

for preparation thereof

Novel, biologically active fragments of human antihemophilic factor, AB processes for their preparation, pharmaceutical preparations containing them and the use of such fragments in the treatment of patients suffering from hemophilia.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:

88:36116 USPATFULL

TITLE:

Biologically active fragments of human antihemophilic

factor and method for preparation thereof

INVENTOR(S):

Andersson, Lars-Olof, Knivsta, Sweden

Forsman, Nanna, Jarfalla, Sweden

Larsen, Kerstin E. I., Lidingo, Sweden Lundin, Annelie B., Stockholm, Sweden

Pavlu, Bohdan, Huddinge, Sweden Sandberg, Inga H., Sp.ang.nga, Sweden Sewerin, Karin M., Bromma, Sweden

PATENT ASSIGNEE(S):

KabiVitrum AB, Stockholm, Sweden (non-U.S. corporation)

DATE KIND NUMBER _______

PATENT INFORMATION:

19880607

APPLICATION INFO.:

US 4749780 US 1986-835914

19860304 (6)

NUMBER DATE

PRIORITY INFORMATION:

SE 1985-1050 19850305

DOCUMENT TYPE:

Utility

FILE SEGMENT:

Granted

PRIMARY EXAMINER:

PRIMARY EXAMINER: Phillips, Delbert R. ASSISTANT EXAMINER: Nutter, Nathan M.

LEGAL REPRESENTATIVE: Pollock, Vande Sande & Priddy

NUMBER OF CLAIMS:

EXEMPLARY CLAIM:

6

NUMBER OF DRAWINGS:

5 Drawing Figure(s); 3 Drawing Page(s)

LINE COUNT:

608

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 25 OF 44 USPATFULL on STN L4

Ultrapurification of factor VIII using monoclonal antibodies TI

A method of preparing high purity procoagulant protein comprising the AB steps of (a) adsorbing a VIII:C/VIII:RP complex from a plasma or commercial concentrate source of factor VIII onto agarose beads bound to a monoclonal antibody specific to VIII:RP, (b) eluting VIII:C with a salt solution, (c) adsorbing the eluted VIII:C on an animohexyl agarose column and eluting the VIII:C with a salt solution.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:

82:57885 USPATFULL

TITLE:

Ultrapurification of factor VIII using monoclonal

INVENTOR(S):

Zimmerman, Theodore S., La Jolla, CA, United States

Fulcher, Carol A., La Jolla, CA, United States

PATENT ASSIGNEE(S):

Scripps Clinic and Research Foundation, La Jolla, CA,

United States (U.S. corporation)

NUMBER KIND DATE US 4361509 19821130 PATENT INFORMATION: APPLICATION INFO.: US 1981-330105 19811214 (6)

DOCUMENT TYPE:

Utility

Granted FILE SEGMENT:

Schain, Howard E. PRIMARY EXAMINER:

NUMBER OF CLAIMS: 16 EXEMPLARY CLAIM: 596 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 26 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. L4

Application of a new statistical approach to optimize the TI immunopurification of antihemophilia A factor.

Our aim was to optimize the immunopurification process of human factor AB VIII. This purification was performed using a mouse monoclonal anti-factor VIII light-chain antibody. Previous dissociation of the factor VIII-von Willebrand

factor complex with CaCl2 led to a 50% increase of the factor VIII adsorption on the immunosorbent. The optimization of the elution step required the analysis of the effects of two parameters, pH and ionic strength, on four different responses: elution yield, concentration, specific activity and stability of factor VIII. For this purpose, a multifunctional method using Doehlert matrices for statistically designed experiments was applied. This methodology allowed us to obtain, with only seven experiments, a 60% increase of the elution yield and a two-fold increase of the specific activity of factor VIII.

93041514 EMBASE ACCESSION NUMBER:

DOCUMENT NUMBER:

1993041514

TITLE:

Application of a new statistical approach to optimize the

immunopurification of antihemophilia A factor.

AUTHOR:

Bihoreau N.; Layet S.; Fontaine-Aupart M.P.; Paolantonacci

Ρ.

CORPORATE SOURCE:

Centre Nat. de Transfusion Sanguine, 3 Avenue des

Tropiques, 91943 Les Ulis Cedex, France

SOURCE:

Journal of Chromatography - Biomedical Applications, (1993)

612/1 (49-56).

Netherlands

ISSN: 0378-4347 CODEN: JCBADL

COUNTRY:

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 025

Hematology

029 Clinical Biochemistry 037 Drug Literature Index

LANGUAGE: English SUMMARY LANGUAGE: English

- ANSWER 27 OF 44 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. L4
- Characteristics of the von Willebrand factor in virus inactivated F VIII TT concentrates: The impact of heat treatment.
- The known transmission of viral diseases, particularly AIDS (HIV, LAV, AB HTLV-III), has led to the mandatory use of virus-inactivated coagulation factor concentrates for treatment of bleeding disorders due to deficient or abnormal synthesis of the factor VIII/von

Willebrand factor complex. The present

investigation was undertaken to study the influence of heat-treatment on the von Willebrand factor (vWf). Using normal plasma as reference material, we studied the influence of low-purification steps in a simple cryo-plasma and a unrefined freeze-dried cryoprecipitate. For comparison, non-heated and heat-inactivated concentrates of different manufacture representing varying heat-treatment protocols were studied using quantitation of von Willebrand factor antigen (vWf:Ag) by electroimmunoassay and ELISA, and investigation of vWf multimeric composition. A locally produced factor VIII concentrate was studied before and after exposure to 68°C for 72 hours (dry state). Whenever possible, commercial preparations manufactured prior to the heat-treatment era were compared with the present product. The locally produced high

purity concentrate elicited only minor changes in oligomeric satellite pattern, which did not change after dry heat exposure. In principle, no major differences were found between non-heated and pasteurized commercial concentrates of same manufactural origin.

ACCESSION NUMBER:

87163210 EMBASE

DOCUMENT NUMBER:

1987163210

TITLE:

Characteristics of the von Willebrand factor in virus inactivated F VIII concentrates: The impact of heat

treatment.

AUTHOR:

Ingerslev J.; Bukh A.; Wallevik K.; et al.

CORPORATE SOURCE:

Department of Clinical Immunology, University Hospital

Aarhus, DK-8000 Aarhus C, Denmark

SOURCE:

Thrombosis Research, (1987) 47/2 (175-182).

CODEN: THBRAA

COUNTRY:

United States

DOCUMENT TYPE:

Journal

FILE SEGMENT:

047 Virology

025

LANGUAGE:

English

- ANSWER 28 OF 44 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN L4
- Application of a new statistical approach to optimize the ΤI

Hematology

immunopurification of antihemophilia A factor.

AB Our aim was to optimize the immunopurification process of human factor This purification was performed using a mouse monoclonal anti-factor VIII light-chain antibody. Previous dissociation of the factor VIII-von Willebrand

factor complex with CaCl-2 led to a 50% increase of the factor VIII adsorption on the immunosorbent. The optimization of the elution step required the analysis of the effects of two parameters, pH and ionic strength, on four different responses: elution yield, concentration, specific activity and stability of factor VIII. For this purpose, a multifunctional method using Doehlert matrices for statistically designed experiments was applied. This methodology allowed us to obtain, with only seven experiments, a 60% increase of the elution yield and a two-fold increase of the specific activity of factor VIII.

ACCESSION NUMBER: DOCUMENT NUMBER:

1993:207726 BIOSIS PREV199395108951

TITLE:

Application of a new statistical approach to optimize the

immunopurification of antihemophilia A factor.

AUTHOR (S):

Bihoreau, N. [Reprint author]; Layet, S.; Fontaine-Aupart,

M. P.; Paolantonacci, P.

CORPORATE SOURCE:

Centre National de Transfusion Sanguine, 3 Avenue des

Tropiques, B.P. 100, 91943 Les Ulis Cedex, France

SOURCE:

Journal of Chromatography Biomedical Applications, (1993)

Vol. 612, No. 1, pp. 49-56.

DOCUMENT TYPE:

Article

LANGUAGE:

English

ENTRY DATE:

Entered STN: 23 Apr 1993

Last Updated on STN: 24 Apr 1993

- ANSWER 29 OF 44 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN L4ΤI CHARACTERISTICS OF THE VON WILLEBRAND FACTOR IN VIRUS INACTIVATED F VIII CONCENTRATES THE IMPACT OF HEAT TREATMENT.
- AB The known transmission of viral diseases, particularly AIDS(HIV, LAV, HTLV-III), has led to the mandatory use of virus-inactivated coagulation factor concentrates for treatment of bleeding disorders due to deficient or abnormal synthesis of the factor VIII/von

Willebrand factor complex. The present

investigation was undertaken to study the influence of heat-treatment on the von Willebrand factor (vWf). Using normal plasma as reference material, we studied the influence of low-purification steps in a simple cryo-plasma and a unrefined freeze-dried cryoprecipitate. comparison, non-heated and heat-inactivated concentrates of different

manufacture representing varying heat-treatment protocols were studied using quantitation of von Willebrand factor antigen (vWf:Aq) by electroimmunoassay and ELISA, and investigation of vWf multimeric composition. A locally produced factor VIII concentrate was studied before and after exposure to 68° C for 72 hours (dry state). Whenever possible, commercial preparations manufactured prior to the heat-treatment era were compared with the present product. The locally produced high purity concentrate elicited only minor changes in oligomeric satellite pattern, which did not change after dry heat exposure. principle, no major differences were found between non-heated and pasteurized commercial concentrates of same maufactural origin.

ACCESSION NUMBER:

1987:380664 BIOSIS

DOCUMENT NUMBER:

PREV198784067161; BA84:67161

TITLE:

CHARACTERISTICS OF THE VON WILLEBRAND FACTOR IN VIRUS

INACTIVATED F VIII CONCENTRATES THE IMPACT OF HEAT

TREATMENT.

AUTHOR (S):

INGERSLEV J [Reprint author]; BUKH A; WALLEVIK K; MOLLER N

P H; STENBJERG S

CORPORATE SOURCE:

DEP CLINICAL IMMUNOL, UNIV HOSP AARHUS, DK-8000 AARHUS C,

DENMARK

SOURCE:

Thrombosis Research, (1987) Vol. 47, No. 2, pp. 175-182.

CODEN: THBRAA. ISSN: 0049-3848.

DOCUMENT TYPE:

Article

FILE SEGMENT:

BA **ENGLISH**

LANGUAGE:

Entered STN: 5 Sep 1987

ENTRY DATE:

Last Updated on STN: 5 Sep 1987

ANSWER 30 OF 44 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN L4

Simple, quick and high-yielding purification of blood TT coagulation factor VIII and its von Willebrand factor complex from highly concentrated solution in high purity, for use as anti-thrombotic.

AN 2000-647421 [62] WPIDS

WO 200061633 A UPAB: 20001130 AB

> NOVELTY - A method for purifying blood coagulation factor VIII/von Willebrand factor

complex comprises mixing a solution containing the complex with a gel and then separating and removing the gel from the solution.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method for purifying blood coagulation factor VIII comprising the dissociation of the complex before ultrafiltration of the mixture.

ACTIVITY - Thrombolytic.

MECHANISM OF ACTION - Anti-thrombotic agent.

USE - The prepared blood coagulation factor VIII can be used as an anti-thrombotic.

ADVANTAGE - The method is simple, quick and high yielding to give blood coagulation factor VIII in high purity. Dwq.0/0

ACCESSION NUMBER:

2000-647421 [62] WPIDS

DOC. NO. CPI:

C2000-195911

TITLE:

Simple, quick and high-yielding purification of

blood coagulation factor VIII and its von Willebrand factor complex from highly concentrated solution in high

purity, for use as anti-thrombotic.

DERWENT CLASS:

INVENTOR(S): HOSOKAWA, K; NAGATA, M; SUZUKI, T

PATENT ASSIGNEE(S):

(CHCC) CHISSO CORP; (FUJO) FUJIMORI KOGYO KK; (FUJO)

FUJIMORI IND CO LTD

COUNTRY COUNT:

92

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG WO 2000061633 Al 20001019 (200062)* JA

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI

SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000036767 A 20001114 (200108) JP 2000611574 X 20020723 (200263)

JP 2002348300 A 20021204 (200310)

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|------|----------------|----------|
| WO 2000061633 | A1 | WO 2000-JP2350 | 20000411 |
| AU 2000036767 | A | AU 2000-36767 | 20000411 |
| JP 2000611574 | X | JP 2000-611574 | 20000411 |
| | | WO 2000-JP2350 | 20000411 |
| JP 2002348300 | A | JP 1999-104587 | 19990412 |

FILING DETAILS:

| PATENT NO |) KI | ND | PATENT | NO |
|------------------------|------|----------------|----------------------|----|
| AU 200003 JP 200061 | | Based Based | 200006 200006 | |

PRIORITY APPLN. INFO: JP 1999-104587 19990412

L4 ANSWER 31 OF 44 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

TI Extracting factor VIII - von

Willebrand factor complex from plasma -

comprises stabilisation, selective absorption, extraction and purification, used for treatment of haemophilia A.

AN 1994-177817 [22] WPIDS

AB EP 600480 A UPAB: 19940722

A process for extracting Factor VIII - von willebrand factor (FVIII:C-FvW) complex from total human plasma comprises: (a) stabilising unfrozen plasma (at room temperature) with antiprotease, or a basic amino acids or wino acids, containing thiolic or indolic gps.; diluted in sterile and approgenic distilled water, in a volume of Ca, 1/2 to 1/10th of the volume of the plasma; (b) treating the mixture with an anionic exchange resin conditioned to separate the factors constituting the protrombinic compled (PTC); (c) stabilising the PTC plasma supernatant with heparin and feeding into a chromatographic column containing an anionic exchange resin suitably conditioned; (d) eluting the adsorbed Factor VIII:C - FvW complex upon the column and collecting the solution and stabilising it with heparin and polyethylene glycol (PEG) and treating it with an aluminium hydroxide, Al (OH) 3, suspension; (e) filtering the supernatant containing Factor VIII: C-FVW and restoring osmolarity conditions in the solution, then subjecting it to viral inactivation; (f) feeding the solution into a chromatographic column, containing a conditioned cationic exchange resin; and (g) eluting the adsorbed Factor VIII: C-FVW complex and bringing the solution obtained to physiologic condition, concentrate and dispensing into vials and lyophilisating.

USE - This method is useful for producing large quantities of Factor VIII concentrates for prophylaxis and treatment of haemophilia A.

Dwg.0/0

ACCESSION NUMBER:

1994-177817 [22] WPIDS

DOC. NO. CPI:

C1994-081287

TITLE:

Extracting factor VIII - von Willebrand factor complex

from plasma - comprises stabilisation, selective absorption, extraction and purification, used

for treatment of haemophilia A.

DERWENT CLASS:

B₀4

INVENTOR (S):

ARRIGHI, S; BORRI, M G; BUCCI, E

PATENT ASSIGNEE(S):

(AIMA-N) AIMA-DERIVATI SPA; (ISTS) SCLAVO SPA; (ISIS-N)

ISI IST SIEROVACCINOGENO ITAL SPA

COUNTRY COUNT:

PATENT INFORMATION:

| PATENT NO | KIND DATE | WEEK LA | PG |
|-------------|-------------|--------------|----|
| EP 600480 | A2 19940608 | (199422)* EN | 5 |
| R: AT CH DE | DK ES FR GB | IT LI NL SE | |
| EP 600480 | A3 19941123 | (199536) | |
| IT 1256622 | B 19951212 | (199627) | |
| EP 600480 | B1 20000906 | (200044) EN | |
| R: AT CH DE | DK ES FR GB | IT LI NL SE | |
| DE 69329371 | E 20001012 | (200059) | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|--------------------------|----------|----------------------------------|----------------------|
| EP 600480 EP 600480 | A2 A3 | EP 1993-119439 EP 1993-119439 | 19931202 19931202 |
| IT 1256622 | В | IT 1992-MI2778 | 19921204 |
| EP 600480 DE 69329371 | B1 E | EP 1993-119439 DE 1993-629371 | 19931202 19931202 |
| 22 070270 | | EP 1993-119439 | 19931202 |

FILING DETAILS:

| PATENT NO | KI | ND | | | 1 | PATENT | NO |
|-------------|----|-------|----|---|----|------------|----|
| | | | | | | - - | |
| DE 69329371 | E | Based | on | • | EΡ | 600480 |) |

PRIORITY APPLN. INFO: IT 1992-MI2778 19921204

ANSWER 32 OF 44 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN L4

Improved purificn. of von Willebrand Factor - by mild incubation step to TI increase therapeutic activity.

AN 1991-124951 [17] WPIDS

1988-292490 [41]; 1996-200346 [20]; 1998-109871 [10] CR

5006642 A UPAB: 19980309 AΒ

In a method for increasing the therapeutic activity of von Willebrand Factor, an essentially purified von Willebrand Factor is obtd. by adsorbing a Factor VIII/von

Willebrand Factor complex obtd. from plasma

or commercial concentrate source onto particles bound to a monoclonal or polyclonal antibody specific to von Willebrand Factor; first eluting Factor VIII from the particles bound to a monoclonal or polyclonal antibody specifc to von Willebrand Factor; first eluting Factor VIII from the particles; next eluting von Willebrand Factor from the particles by washing the particles with a 0.05 M to 5 M aqueous solution of a chaotropic agent; and separating the von Willebrand factor from the chaotropic agent. The essentially purified von Willebrand Factor is then incubated at a

temperature of 20deg.C to 55deg.C for 1 to 30 hours

WPIDS ACCESSION NUMBER: 1991-124951 [17]

1988-292490 [41]; 1996-200346 [20]; 1998-109871 [10] CROSS REFERENCE:

C1991-053933 DOC. NO. CPI:

Improved purificn. of von Willebrand Factor - by mild TITLE:

incubation step to increase therapeutic activity.

DERWENT CLASS: B04

FARB, D L; NEWMAN, J INVENTOR(S):

PATENT ASSIGNEE(S): (RHON) RHONE-POULENC RORER COUNTRY COUNT:

1

PATENT INFORMATION:

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|------------|------|----------------|----------|
| | | | |
| US 5006642 | Α | US 1988-205881 | 19880613 |

PRIORITY APPLN. INFO: US 1988-205881 19880613; US 1987-67990 19870629

L4 ANSWER 33 OF 44 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

Preparation of factor VIII-von-willebrand
factor complex concentrate - by pre-purifying whole
plasma with barium chloride and aluminium hydroxide then purifying by
chromatography on anion exchange resin.

AN 1991-075455 [11] WPIDS

AB EP 416983 A UPAB: 19930928

A process for the preparation of a stable Factor VIII-von Willebrand factor concentrate with a high specific activity is claimed. The process involves pre-purifying whole blood plasma by a double treatment with barium chloride and aluminium hydroxide and purifying by chromatography using an anion exchange resin which allows retention of very large molecules. The plasma may be fresh or frozen. The plasma may be added to a stabilising mixture containing 2.0-2 micro/ml heparin, 1-5 mM EDTA and 1-10 mM CaCl2, optionally with glucose at a concentration of 5-60 g/l. The pre-purification preferably comprises precipitation from barium chloride followed by centrifugation and recuperation of the supernatant; adsorption on aluminium hydroxide gel followed by cold centrifugation and recuperation of the supernatant, and finally a de-salting treatment. Factor VIII-von Willebrand factor concentrates and protein concentrates derived from the plasma are also claimed, as is their therapeutic usage.

USE/ADVANTAGE - In the treatment of haemophilia the process is simple and gives a high purity, stable concentration in good yield. Since the plasma does not need prior cryoprecipitation, loses of Factor VIII are reduced. The pre-purification step eliminates the constituents of the prothrombinic complex (Factors II, VII, IX, X).

ABEO EP 416983 B UPAB: 19931118

Process for preparing a stable concentrate of the Factor VIII-von Willebrand factor having high specific activity, characterised in that a total plasma is subjected to pre-purificatin by a double treatment which comprises precipitation with barium chloride and adsorption on aluminium hydroxide gel and to purification by chromatography on an anion exchange gel permitting the retention of very large molecules.

Dwg.0/0

ABEQ US 5679776 A UPAB: 19971209

A process for preparing a stable concentrate of a Factor VIII-von Willebrand factor complex which comprises:

- (a) contacting non-cryoprecipitated total plasma with barium chloride and collecting a first supernatant;
 - (b) contacting said first supernatant with aluminum hydroxide gel;
 - (c) centrifuging and collecting a second supernatant;
 - (d) de-salting said second supernatant;
- (e) contacting said second supernatant with an anion exchange gel, comprising a copolymer of oligoethylene glycol, glycine methacrylate, and

pentaerythrol-dimethacrylate; and

(f) collecting said stable concentrate of Factor

VIII-von Willebrand factor

complex.

Dwg.0/0 ACCESSION NUMBER:

WPIDS 1991-075455 [11]

DOC. NO. CPI:

C1991-032009

TITLE:

Preparation of factor VIII-von-

willebrand factor complex

concentrate - by pre-purifying whole plasma with barium chloride and aluminium hydroxide then purifying by

chromatography on anion exchange resin.

DERWENT CLASS:

INVENTOR(S):

BURNOUF, T; BURNOUF-RADOSEVICH, M; BURNOUF, THIERRY B T;

BURNOUFRAD, M

PATENT ASSÍGNEE(S):

(REGI-N) CENT REGIONAL TRANSFUSION SANGUINE; (REGI-N) CENT REG TRANS SANG; (BURN-I) BURNOUF-RADOSEVICH;

(REGI-N) CENT REGIONAL TRANS; (REGI-N) CENT REGIONAL

TRANSFUSION SANGUINE LILLE

COUNTRY COUNT: PATENT INFORMATION:

| PATENT NO | KI | ND DATE | WEEK | LA | PG |
|--------------------------|----|----------|-----------|-------|-------|
| EP 416983 R: AT BE CH | DE | | | LU NL | SE |
| NO 9003865 CA 2024667 | | | (199120) | | |
| FR 2651437 | A | | (199120) | | |
| FI 9004381 | | | (199123) | | |
| | T | | (199147) | | |
| BR 9004626 | | | • | | |
| AU 9062218 | | | (199220) | | |
| JP 04124199 | | | (199223)# | | 7 |
| | | 19920206 | | | |
| CZ 9004312 | А3 | | (199319) | | |
| EP 416983 | В1 | | (199330) | FR | 9 |
| R: AT BE CH | DE | DK ES FR | GB GR IT | LI LU | NL SE |
| DE 69002427 | E | 19930902 | (199336) | | |
| CZ 277939 | | | • | | |
| ES 2057475 | | | | | |
| RU 2025129 | C1 | | (199531) | | 6 |
| FI 95654 | В | | (199601) | | |
| NO 178716 | | | (199611) | | _ |
| US 5679776 | | | (199748) | | 5 |
| 010 = 7 - 0 - 0 | В6 | | (199850) | | |
| | | 19981007 | | | _ |
| JP 2931655 | | | (199937)# | | 6 |
| - · | | | (200038)# | | |
| CA 2024667 | C | 20010731 | (200147) | EN | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|--------------------------|----------|--------------------------------|----------------------|
| EP 416983 | A | EP 1990-402395 | 19900830 |
| FR 2651437 AU 9062218 | A A | FR 1989-11567 AU 1990-62218 | 19890905 19900906 |
| DD 298110 | A5 | DD 1990-343869 | 19900905 |
| CZ 9004312 EP 416983 | A3 B1 | CS 1990-4312 EP 1990-402395 | 19900905 19900830 |
| DE 69002427 | E | DE 1990-602427 | 19900830 |
| CZ 277939 | В6 | EP 1990-402395 CS 1990-4312 | 19900830 19900905 |

| ES | 2057475 | Т3 | ΕP | 1990-402395 | 19900830 |
|----|---------|----|----|--------------|----------|
| RU | 2025129 | C1 | SU | 1990-4831275 | 19900904 |
| FI | 95654 | В | FI | 1990-4381 | 19900905 |
| NO | 178716 | В | NO | 1990-3865 | 19900905 |
| US | 5679776 | A | US | 1990-577368 | 19900905 |
| SK | 279367 | B6 | CS | 1990-4312 | 19900905 |
| SK | 9004312 | A3 | CS | 1990-4312 | 19900905 |
| JP | 2931655 | B2 | JP | 1990-240177 | 19900912 |
| KR | 168415 | B1 | KR | 1990-14264 | 19900910 |
| CA | 2024667 | C | CA | 1990-2024667 | 19900905 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO | | | |
|-------------|-------------------|-------------|--|--|--|
| DE 69002427 | E Based on | EP 416983 | | | |
| CZ 277939 | B6 Previous Publ. | CS 9004312 | | | |
| ES 2057475 | T3 Based on | EP 416983 | | | |
| FI 95654 | B Previous Publ. | FI 9004381 | | | |
| NO 178716 | B Previous Publ. | NO 9003865 | | | |
| SK 279367 | B6 Previous Publ. | SK 9004312 | | | |
| JP 2931655 | B2 Previous Publ. | JP 04124199 | | | |

PRIORITY APPLN. INFO: FR 1989-11567 19890905; KR 1990-14264 19900910

L4 ANSWER 34 OF 44 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

TI Isolation of the factor VIII - von

Willebrand factor complex directly from plasma by gel filtration

Ahigh capacity gel filtration system was developed with the purpose of isolating factor VIII (FVIII) and von Willebrand factor (VWF) directly from plasma in significantly higher yields than obtained by cryoprecipitation, the technique most commonly used to recover FVIII-VWF from human plasma. After laboratory-scale gel filtration of plasma, a FVIII-containing fraction was collected containing about 90% of FVIII in the applied plasma and with almost tenfold higher purity than that obtained by cryoprecipitation. The gel filtration step has been scaled up for use as the initial step in the manufacturing process for a FVIII preparation (Nordiate). (C) 1998 Elsevier Science B.V. All rights reserved.

ACCESSION NUMBER: 1998:792752 SCISEARCH

THE GENUINE ARTICLE: 127HP

TITLE: Isolation of the factor VIII -

von Willebrand factor

complex directly from plasma by gel filtration

AUTHOR: Kaersgaard P (Reprint); Barington K A

CORPORATE SOURCE: HEMASURE DENMARK AS, SAUNTESVEJ 13, DK-2820 GENTOFTE,

DENMARK (Reprint)

COUNTRY OF AUTHOR: DENMARK

SOURCE: JOURNAL OF CHROMATOGRAPHY B, (18 SEP 1998) Vol. 715, No.

2, pp. 357-367.

Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE

AMSTERDAM, NETHERLANDS.

ISSN: 0378-4347.
Article: Journal

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 34

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L4 ANSWER 35 OF 44 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

TI APPLICATION OF A NEW STATISTICAL APPROACH TO OPTIMIZE THE IMMUNOPURIFICATION OF ANTIHEMOPHILIA-A FACTOR

Our aim was to optimize the immunopurification process of human factor AB VIII. This purification was performed using a mouse monoclonal anti-factor VIII light-chain antibody. Previous dissociation of the factor VIII-von Willebrand

factor complex with CaCl2 led to a 50% increase of the factor VIII adsorption on the immunosorbent. The optimization of the elution step required the analysis of the effects of two parameters, pH and ionic strength, on four different responses: elution yield, concentration, specific activity and stability of factor VIII. For this purpose, a multifunctional method using Doehlert matrices for statistically designed experiments was applied. This methodology allowed us to obtain, with only seven experiments, a 60% increase of the elution yield and a two-fold increase of the specific activity of factor VIII.

93:122175 SCISEARCH ACCESSION NUMBER:

THE GENUINE ARTICLE: KN624

APPLICATION OF A NEW STATISTICAL APPROACH TO OPTIMIZE THE TTTLE:

IMMUNOPURIFICATION OF ANTIHEMOPHILIA-A FACTOR

BIHOREAU N (Reprint); LAYET S; FONTAINEAUPART M P; AUTHOR:

PAOLANTONACCI P

INST MERIEUX, CTR NATL TRANSFUS SANGUINE, 3 AVE TROPIQUES. CORPORATE SOURCE:

BP 100, F-91943 LES ULIS, FRANCE (Reprint); UNIV PARIS 11,

PHOTOPHYS MOLEC LAB, UPR 3361, F-91405 ORSAY, FRANCE

COUNTRY OF AUTHOR:

FRANCE

JOURNAL OF CHROMATOGRAPHY-BIOMEDICAL APPLICATIONS, (29 JAN SOURCE:

1993) Vol. 612, No. 1, pp. 49-56.

ISSN: 0378-4347.

DOCUMENT TYPE:

Article; Journal LIFE

FILE SEGMENT: LANGUAGE:

ENGLISH

REFERENCE COUNT:

30

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

ANSWER 36 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN L4

Blood coagulation factor VIII and blood coagulation factor TI

VIII/von Willebrand factor

complex purification method with gel filtration

A method for purifying a blood coagulation factor VIII/Von Willebrand factor (FVIII/vWF) complex and blood coagulation factor VIII (FVIII) via a simple step even from a solution containing a large amount of the blood coagulation

factor VIII/Von Willebrand

factor complex, is disclosed. This method comprises

mixing a solution containing the blood coagulation factor VIII

/Von Willebrand factor complex

with a gel and then separating and removing the gel from the solution Use of

dry

gel and gel filtration chromatog. possibly in combination with anhydro-thrombin affinity chromatog. in this method is claimed. FVIII/vWF complex was purified using dry Sephacryl-300 gel and Sepharose 6B gel filtration chromatog., dry Sepharose 6B and Sephacryl-400 gel filtration chromatog., or Sephacryl-4B gel filtration chromatog. Impurities such as fibrinogen and fibronectin were removed.

ACCESSION NUMBER:

2000:742141 HCAPLUS

DOCUMENT NUMBER:

133:278346

TITLE:

Blood coagulation factor VIII and blood coagulation

factor VIII/von

Willebrand factor complex

purification method with gel filtration

INVENTOR(S):

Hosokawa, Kazuya; Suzuki, Toyoaki; Nagata, Masanori

PATENT ASSIGNEE(S):

Fujimori Kogyo Co., Ltd., Japan

SOURCE:

PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE:

Patent Japanese had date

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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APPLICATION NO. DATE
     PATENT NO.
                         KIND DATE
                                                 _____
                                                 WO 2000-JP2350
                         A1
                               20001019
                                                                    20000411
     WO 2000061633
          W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
              CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
              SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
               ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
              DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
               CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                               JP 1999-104587
                                                                    19990412
                         A2 20021204
     JP 2002348300
                                                                A 19990412
PRIORITY APPLN. INFO.:
                                             JP 1999-104587
                                   THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS
                            32
REFERENCE COUNT:
                                   RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
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- L4 ANSWER 37 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
- TI Chromatographic purification of factor VIII/

von Willebrand factor complex

The invention relates to a method for the production of factor VIII:C/von Willebrand factor complex from plasma or a plasma fraction by chromatog. on a cation exchanger, wherein the factor VIII:C/von Willebrand factor complex is obtained with at least 300 times the purity of the plasma and the yield of factor VIII:C and the von Willebrand factor is at least 50 % in relation to cryoppts. or analogous plasma fractions. The purification is achieved in a single step; the process is combined with antiviral treatment, e.g. addition of organic solvents and/or detergents, ultrafiltration etc. Thus factor VIII/von

Willebrand factor complex was purified from

cryoppt. with 62%/68% yield and a 450-fold purification using Fractogel EMD-SO3- and a solution of Triton X100 and tri(n-butyl)phosphate.

ACCESSION NUMBER:

1999:566081 HCAPLUS

DOCUMENT NUMBER:

131:167367

TITLE:

Chromatographic purification of

factor VIII/von

Willebrand factor complex

INVENTOR(S):

Linnau, Yendra; Schonhofer, Wolfgang Immuno Aktiengesellschaft, Austria

PATENT ASSIGNEE(S): SOURCE:

PCT Int. Appl., 15 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

German

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PA. | rent 1 | NO. | | KI | ND : | DATE | | | A) | PPLI | CATI | ON NO | ο. | DATE | | | | |
|-----|--------|-----|-----|-----|------|------|------|-----|-----|------|-------|-------|-----|------|------|-----|-----|----|
| | | | | | | | | | | | | | | | | | | |
| WO | 9943 | 712 | | A | 1 | 1999 | 0902 | | W | 0 19 | 99-A' | Г48 | | 1999 | 0225 | | | |
| | W: | AL, | AM, | ΑT, | AU, | AZ, | BA, | BB, | BG, | BR, | BY, | CA, | CH, | CN, | CU, | CZ, | DE, | |
| | | DK, | EE, | ES, | FI, | GB, | GD, | GE, | GH, | GM, | HR, | ΗU, | ID, | IL, | IN, | IS, | JP, | |
| | | KE, | KG, | KΡ, | KR, | ΚZ, | LC, | LK, | LR, | LS, | LT, | LU, | LV, | MD, | MG, | MK, | MN, | |
| | | MW, | MX, | NO, | NZ, | PL, | PT, | RO, | RU, | SD, | SE, | SG, | SI, | SK, | SL, | ТJ, | TM, | |
| | | TR, | TT, | UA, | ŪĠ, | US, | UZ, | VN, | YU, | ZW, | AM, | ΑZ, | BY, | KG, | ΚZ, | MD, | RU, | |
| | | ТJ, | TM | | | | | | | | | | | | | | | |
| | RW: | GH, | GM, | KΕ, | LS, | MW, | SD, | SL, | SZ, | ŪĠ, | ZW, | AT, | ΒE, | CH, | CY, | DE, | DK, | |
| | | ES, | FI, | FR, | GB, | GR, | ΙE, | IT, | LU, | MC, | NL, | PT, | SE, | BF, | ВJ, | CF, | CG, | |
| | | CI, | CM, | GΑ, | GN, | GW, | ML, | MR, | NE, | SN, | TD, | TG | | | | | | |
| WO | 9838 | 220 | | A: | 1 | 1998 | 0903 | | W | 0 19 | 98-A' | Г43 | | 1998 | 0227 | | | |
| | W: | AU, | BR, | CA, | CZ, | ΗU, | IL, | JP, | MX, | NO, | PL, | RU, | SI, | SK, | US | | | |
| | RW: | ΑT, | BE, | CH, | DE, | DK, | ES, | FI, | FR, | GB, | GR, | ΙE, | IT, | LU, | MC, | NL, | PT, | SE |

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AT 1998-866
                                                             19980520
     AT 9800866
                       Α
                            20010415
     AT 408443
                       В
                            20011126
                            19990915
                                           AU 1999-25030
                                                             19990225
     AU 9925030
                       Α1
                                           EP 1999-904614
     EP 1056779
                       A1
                            20001206
                                                             19990225
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
                                           JP 2000-533462
     JP 2002504561
                       Т2
                            20020212
                                                            19990225
     US 6605222
                            20030812
                                           US 2001-623245
                                                            20010319
                       B1
PRIORITY APPLN. INFO.:
                                        WO 1998-AT43
                                                         W 19980227
                                        AT 1998-866
                                                         A 19980520
                                        AT 1997-338
                                                         A 19970227
                                        WO 1999-AT48
                                                         W 19990225
                               THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                         7
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L4
     ANSWER 38 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
     Purification of factor VIII/von
ΤI
     Willebrand factor complex by cation-exchange
     chromatography
     A method of purifying the factor VIII/von Willebrand factor (vWF) complex
AΒ
     by cation-exchange chromatog. is described. Complex bound to a
     cation-exchanger is eluted with a salt gradient to release factor VIII/vWF
     complex especially complexes containing vWF multimers. The method can be used
on
     crude prepns., such as blood cryoppts., but is most effective when the
     protein is partially purified, e.g. by anion-exchange chromatog. The
     preferred cation exchanger is an acid form of Fractogel EMD.
     Purifications of >300-fold and yields of >50% are obtained.
ACCESSION NUMBER:
                         1998:608647 HCAPLUS
DOCUMENT NUMBER:
                         129:213514
TITLE:
                         Purification of factor
                         VIII/von Willebrand
                         factor complex by cation-exchange
                         chromatography
INVENTOR(S):
                         Mitterer, Artur; Fischer, Bernhard; Schonberger,
                         Oyving L.; Thomas-Urban, Kathrin; Dorner, Friedrich;
                         Eibl, Johann
                         Immuno A.-G., Austria
PATENT ASSIGNEE(S):
                         PCT Int. Appl., 31 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
                         German
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                     KIND DATE
                                           APPLICATION NO.
                                                            DATE
                            19980903
                                           WO 1998-AT43
     WO 9838220
                      A1
                                                            19980227
        W: AU, BR, CA, CZ, HU, IL, JP, MX, NO, PL, RU, SI, SK, US
         RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
    AT 9700338
                            19990915
                                           AT 1997-338
                                                            19970227
                      Α
    AT 406373
                       В
                            20000425
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                                           AU 1998-60806
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                            19990915
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PRIORITY APPLN. INFO.:
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                                                         A 19970227
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                                        WO 1999-AT48
                                                         W 19990225
                                        US 2000-367459
                                                         A3 20000508
REFERENCE COUNT:
                               THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
     ANSWER 39 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN
L4
     Immunoaffinity purification of von Willebrand factor or
TT
     factor VIII/von Willebrand
     factor complex
AB - A method for obtaining high-purity von Willebrand factor (vWF) or factor
     VIII/vWF complex by immunoaffinity chromatog. is described. VWF or factor
     VIII/vWF complex bound with an immune adsorbing agent is eluted with a
     medium containing a zwitterion, e.g. an amino acid, as an essential active
     part, while preserving the mol. integrity of the vWF or factor VIII/vWF
     complex. The purified factor can be used in the treatment of hemophilia
     A. Monoclonal antibodies were tested for their effectiveness in specific
     and reversible binding of vWF and factor VIII complex. Amino acids were
     tested for their effectiveness in elution of vWF with betaine the most
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effective at neutral pH's and other non-polar also highly effective. ACCESSION NUMBER: 1998:608645 HCAPLUS

DOCUMENT NUMBER: 129:213512

TITLE: Immunoaffinity purification of von

Willebrand factor or factor VIII/

von Willebrand factor

complex

INVENTOR(S): Mitterer, Artur; Fiedler, Christian; Fischer,

Bernhard; Dorner, Friedrich; Eibl, Johann

PATENT ASSIGNEE(S): Immuno A.-G., Austria SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND DATE | APPLICATION NO. DATE |
|---------------|-----------------|--|
| | | |
| WO 9838218 | A1 19980903 | WO 1998-AT33 19980218 |
| W: AU, BR, | CA, CZ, HU, IL, | JP, MX, NO, PL, RU, SI, SK, US |
| RW: AT, BE, | CH, DE, DK, ES, | FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE |
| AT 9700339 | A 20000215 | AT 1997-339 19970227 |
| AT 406867 | B 20001025 | |
| AU 9861998 | Al 19980918 | AU 1998-61998 19980218 |
| AU 734277 | B2 20010607 | |
| EP 1012191 | A1 20000628 | EP 1998-903938 19980218 |
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| JP 2001513762 | T2 20010904 | JP 1998-537055 19980218 |
| NO 9904084 | A 19991019 | NO 1999-4084 19990824 |
| US 6579723 | B1 20030617 | US 1999-367362 19991021 |

PRIORITY APPLN. INFO.: AT 1997-339 A 19970227 WO 1998-AT33 19980218

REFERENCE COUNT: THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS 5 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4ANSWER 40 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN

TT Pilot immunoaffinity purification of factor VIII/vWF complex (preliminary results)

AB A standard purification procedure for the blood Factor VIII/ von Willebrand Factor complex is

119:265807

described. It is based on an immunoaffinity chromatog. protocol.

ACCESSION NUMBER: 1993:665807 HCAPLUS

DOCUMENT NUMBER:

CORPORATE SOURCE:

TITLE:

Pilot immunoaffinity purification of factor

VIII/vWF complex (preliminary results)

AUTHOR (S): Van Wijngaarden, L.; Hoff, H. S.; Koops, K.; Van

Weperen, J. J.; Das, P. C.; Sibinga, C. T. Smit Bio-Intermediair B.V., Groningen, 9700 AL, Neth. Collogue INSERM (1993), 227 (Biotechnology of Blood

SOURCE: Proteins), 109-14

CODEN: CINMDE; ISSN: 0768-3154

DOCUMENT TYPE: Journal English LANGUAGE:

ANSWER 41 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN T,4

Immunoaffinity purification of factor VIII/

von Willebrand factor complex

Preliminary results of the design of an immunoaffinity purification of the AB factor VIII/von Willebrand factor (vWF) complex are summarized. An overview of an approach on the development and screening for an anti-vWF antibody suitable in an immunoaffinity purification system is presented.

ACCESSION NUMBER: 1992:403089 HCAPLUS

DOCUMENT NUMBER:

117:3089

TITLE:

Immunoaffinity purification of

factor VIII/von

Willebrand factor complex

Koops, K.; Hoff, H. S.; Van Weperen, J. J.; Das, P. AUTHOR (S):

CORPORATE SOURCE:

C.; Smit Sibinga, C. T. Bio-Intermediair, Groningen, Neth.

SOURCE:

Developments in Hematology and Immunology (1991),

26 (Coagulation Blood Transfus.), 103-17

CODEN: DHIMDR; ISSN: 0167-9201

DOCUMENT TYPE:

Journal; General Review

LANGUAGE:

English

ANSWER 42 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN T.4

The purification of the VIII/vWF complex using dextran sulfate TΤ Sepharose chromatography

Factor VIII/vWf displays high affinity for matrix-bound dextran sulfate. AB Due attention to the flow rates has to be taken into consideration to achieve maximal binding. Typical yields of vWf:Ag are usually 70-90% expressing biol. activity and of normal multimeric distribution. Factor VIII:C can be copurified with vWf:Ag providing a sufficient concentration of

free

Ca is present at 4°. Higher concns. of Ca (20 mM) lead to blockage of the columns. Normal yields of thrombin-activatable factor VIII are usually 40% VIII:C and 70% VIII:Aq. Alternatively, higher yields of VIII:C can be obtained (80% VIII:C and 100% VIII:Aq) by application of L-lysine gradients but with some loss of resolution between proteins. VIII:C has a vWf-independent affinity for DS. These matrixes demonstrate potential value in the fractionation of plasma or genetically engineered products.

ACCESSION NUMBER: 1990:11822 HCAPLUS

DOCUMENT NUMBER:

112:11822

The purification of the VIII/vWF complex TITLE:

> using dextran sulfate Sepharose chromatography Harrison, P.; Saundry, R. H.; Savidge, G. F.

Rayne Inst., UMDS, London, SE1 7EH, UK CORPORATE SOURCE:

Colloque INSERM (1989), 175 (Biotechnol. Proteines SOURCE:

Plasma), 279-85

CODEN: CINMDE; ISSN: 0768-3154

DOCUMENT TYPE: Journal LANGUAGE: English

AUTHOR (S):

ANSWER 43 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN L4

TI Monoclonal antibody affinity purification of plasma proteins removes viral contaminants

Monoclate is a highly purified Factor VIII prepared by a two column affinity purification process. The procedure employs a monoclonal anti-von Willebrand antibody to purify the Factor VIII-von

Willebrand factor complex from the cryoppt.

and an aminohexyl affinity column to remove any leached murine IqG and effect some addnl. purification Studies with HIV, pseudorabies, sinbus, vesicular stomatitis, and vaccinia viruses demonstrated that the Monoclate manufacturing process reduced each of these viruses by at least 5 logs and that heating at 60° for 30 h resulted in an overall virus titer reduction of more than 9 logs. Monoclate has proven to be an effective therapeutic agent for the treatment of Hemophilia. Monoclate has the added virtue of a lower virus burden and less alloantigens and other proteins. Monoclate can be reconstituted in less than a minute, and because of its high potency and small volume, it can be rapidly infused. The method of monoclonal affinity purification used to prepare Monoclate may prove to be a generic process for reducing the virus load of therapeutic protein prepns.

ACCESSION NUMBER: 1989:619158 HCAPLUS

DOCUMENT NUMBER: 111:219158

Monoclonal antibody affinity purification of TITLE:

plasma proteins removes viral contaminants

AUTHOR (S): Hrinda, M. E.; Tarr, C.; Curry, W.; Newman, J.;

Schreiber, A. B.; D'Alisa, R.

Rorer Biotechnol. Inc., King of Prussia, PA, 19406, CORPORATE SOURCE:

Colloque INSERM (1989), 175 (Biotechnol. Proteines SOURCE:

Plasma), 413-17

CODEN: CINMDE; ISSN: 0768-3154

DOCUMENT TYPE:

Journal LANGUAGE: English

T.4 ANSWER 44 OF 44 HCAPLUS COPYRIGHT 2004 ACS on STN

Purification of factor VIII by monoclonal antibody affinity TT chromatography

Monoclonal antibodies were raised to von Willebrand factor, and linked to AB a solid-phase agarose support. Due to the high affinity of these antibodies for the von Willebrand factor end of the factor

VIII/von Willebrand factor

complex, it was possible to effectively pull out the

factor VIII/von Willebrand

factor complex from com. concs. or cryoppts. The next stage of the process involved eluting the factor VIII portion of the complex from the von Willebrand factor. CaCl2 at a concentration of .apprx.0.25-0.3M was used to elute factor VIII, leaving the von Willebrand factor bound to the monoclonal antibody column. Following concentration by ultrafiltration, trace contaminants, such as von Willebrand factor, fibrinogen, or fibronectin, could be removed by monoclonal antibodies specific for them. Finally, the product was rechromatographed to allow for further purification and concentration The resultant factor VIII preparation had a

concentration in the range 134-1172 units (U)/mL and a specific activity of

U/mg. A refined procedure and some applications are discussed. SSION NUMBER: 1988:434300 HCAPLUS

ACCESSION NUMBER:

DOCUMENT NUMBER:

109:34300

TITLE:

Purification of factor VIII by monoclonal antibody affinity chromatography

AUTHOR (S):

SOURCE:

CORPORATE SOURCE:

Zimmerman, Theodore S. Scripps Clinic Res. Found., La Jolla, CA, 92037, USA Seminars in Hematology (1988), 25(2, Suppl. 1), 25-6

CODEN: SEHEA3; ISSN: 0037-1963

DOCUMENT TYPE:

Journal LANGUAGE: English

Refine Search

Search Results -

| Terms | Documents |
|-------------|-----------|
| 6228613.pn. | 1 |

US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

L13

Refine Search

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| <u>L12</u> | 6307032.pn. | 1 | <u>L12</u> |
| <u>L11</u> | 19 and high molecular weight vWF multimer | 1132985 | <u>L11</u> |
| <u>L10</u> | 11 and L9 | 0 | <u>L10</u> |
| <u>L9</u> | 12 and L8 | 143 | <u>L9</u> |
| <u>L8</u> | 14 and L7 | 143 | <u>L8</u> |
| <u>L7</u> | 15 and L6 | 93994 | <u>L7</u> |
| <u>L6</u> | factor VIII-von Willebrand factor complex | 971739 | <u>L6</u> |
| <u>L5</u> | purification and 13 | 104349 | <u>L5</u> |
| <u>L4</u> | 12 and L3 | 674 | <u>L4</u> |
| <u>L3</u> | factor VIII same2 von Willebrand factor complex | 1055539 | <u>L3</u> |
| <u>L2</u> | Zhou.in. | 1221 | <u>L2</u> |
| <u>L1</u> | 6605222.pn. | 1 | <u>L1</u> |
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US Patents Full-Text Database

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US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

L14

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| <u>L12</u> | 6307032.pn. | 1 | <u>L12</u> | |
| <u>L11</u> | 19 and high molecular weight vWF multimer | 1132985 | <u>L11</u> | |
| <u>L10</u> | 11 and L9 | 0 | <u>L10</u> | |
| <u>L9</u> | 12 and L8 | 143 | <u>L9</u> | |
| <u>L8</u> | 14 and L7 | 143 | <u>L8</u> | |
| <u>L7</u> | 15 and L6 | 93994 | <u>L7</u> | |
| <u>L6</u> | factor VIII-von Willebrand factor complex | 971739 | <u>L6</u> | |
| <u>L5</u> | purification and 13 | 104349 | <u>L5</u> | |
| <u>L4</u> | 12 and L3 | 674 | <u>L4</u> | |
| <u>L3</u> | factor VIII same2 von Willebrand factor complex | 1055539 | <u>L3</u> | |
| <u>L2</u> | Zhou.in. | 1221 | <u>L2</u> | |
| <u>L1</u> | 6605222.pn. | 1 | <u>L1</u> | |
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END OF SEARCH HISTORY